Pergamon

Tetrahedron Letters 40 (1999) 5283–5286

TETRAHEDRON LETTERS

A versatile tandem retro-[1,4]-Brook rearrangement–condensation reaction of *o*-bromoacetophenone silyl enol ethers

Bogdan M. Comanita,† Simon Woo and Alex G. Fallis *

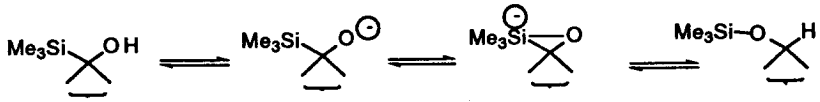
Department of Chemistry, University of Ottawa, 10 Marie Curie, Ottawa, Ontario, Canada, K1N 6N5

Received 11 May 1999; accepted 12 May 1999

Abstract

The retro-[1,4]-Brook rearrangement (also referred to as the West or silyl-Wittig rearrangement) has been employed with acetophenone silyl enol ethers to allow regiospecific migration of the silicon from oxygen to the *ortho* position of the aromatic ring. The enolate that results from this process may be reacted directly with various electrophiles.

The Brook rearrangement is a 1,2-anionic migration of a silyl group from a carbon atom (center) to an oxygen atom.[1,2] The reaction is facilitated by electron withdrawing substituents on the carbon center and proceeds via a pentacoordinate intermediate (Scheme 1). Typically, this occurs under catalytic basic conditions. In general, the strength of the silicon–oxygen bond favors the formation of the silyl ether over the carbosilane. The reverse migration involving the transfer of a silyl substituent from oxygen to a formally anionic carbon is encountered less frequently. This process is referred to as an anti- or retro-Brook,[1,2] or West[3] or silyl-Wittig,[4] rearrangement. The migration can proceed over various distances with carbons at different levels of hybridization. These reactions comprise a family of [1,*n*]-*C* to -*O* or the reverse *O*- to *C*-silyl migrations (Scheme 2). Recently, there has been considerable interest in this extended group of [1,3]-, [1,4]- and [1,5]-oxygen to carbon silyl migrations.[5,6] These sequences have proved useful in a variety of synthetic applications.

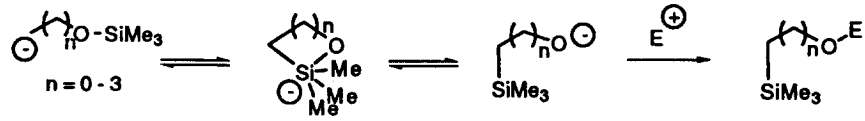


Scheme 1. Standard [1,2]-Brook rearrangement

* Corresponding author.

† Present address: National Research Council Canada, Institute for Chemical Process and Environmental Technology, Montreal Road Campus, Ottawa, Ontario, Canada K1A 0R6.

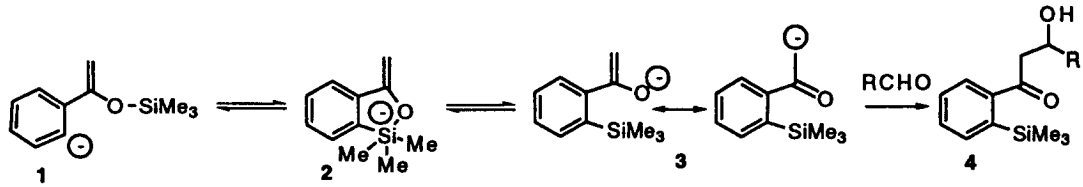
0040-4039/99/$ - see front matter
PII: S0040-4039(99)00963-6



Scheme 2. Retro-[1,*n*]-Brook rearrangement

An important driving force for these rearrangements in the oxygen to carbon direction is the increased stability of the alkoxide anion compared to the carbanion intermediate. In these systems the nature of the counterion may exert a strong influence on the position of the equilibrium. Generally, lithium favors the oxygen–carbon migration and sodium and potassium the formation of the silyl ether. The ease of migration follows the general trend in which the shortest transfer distance is preferred {[1,2]>[1,3]≫[1,4]>[1,5]},[5–7] although the factors responsible for controlling the regioselectivity of the long range equilibria are less well understood and consequently not as readily predictable.

As part of a synthetic project we have developed a remote functionalization sequence which employs a tandem retro-[1,4]-Brook rearrangement/condensation or alkylation reaction protocol to transfer the silyl moiety to the *ortho* position of acetophenone type ketones. This generalized transformation of *ortho*-bromo-acetophenone silyl enol ethers followed by condensation is illustrated in Scheme 3. The generation of a reactive aryl carbanion **1** in association with the formation of the stabilized enolate **3** should provide the driving force for the desired retro-Brook migration. The enolate derived from this process should react directly with electrophiles to provide functionalized methyl ketones. This protocol was required as the direct aldol condensation of the potassium enolate derived from *o*-bromoacetophenone (**5**) with the unstable aldehyde **8** gave only a 12% yield of **9** (X=Br).



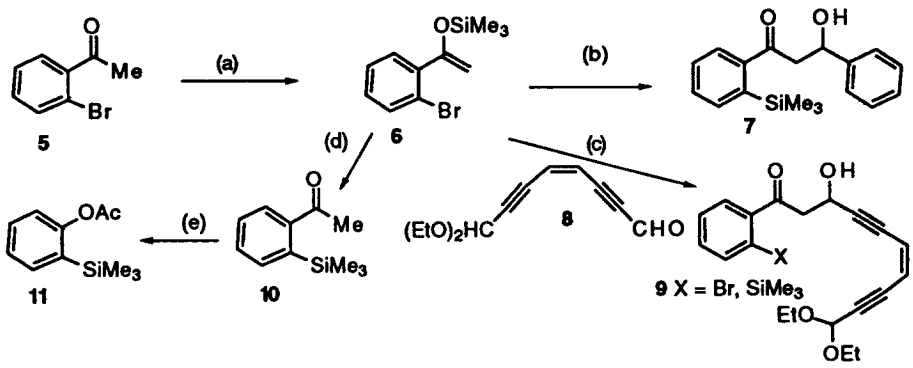
Scheme 3. Tandem retro-[1,4]-Brook rearrangement/condensation

In contrast, when **5** was transformed into the trimethylsilyl enol ether **6**, and halogen–metal exchange effected with butlylithium the anticipated retro-Brook rearrangement occurred rapidly at low temperature (–78°C). Thus, as expected, the crossed aldol condensation product with benzaldehyde afforded ketone **7** in good yield (Scheme 4). Of greater significance this tandem sequence generated enediyne system **9** (X=$SiMe_3$) directly from the unstable aldehyde **8**. In this instance addition of anhydrous cerium trichloride to the lithium enolate was required prior to condensation (Scheme 4).

Previous examples of [1,3]-oxygen to vinyl or aryl migration have been reported.[6] Possibly the closest analogy to the present case, involving the migration to an unsaturated center, is the [1,4]-oxygen to carbon migration in furans. These examples depend on the acidity of the C_2 hydrogen. The formation of the anionic sp^2 hybridized center controls the transfer from an adjacent primary silyl ether.[7a–d]

Controlling the substitution pattern of aromatic rings in complex natural antibiotics such as vancomycin is an area of considerable current interest.[8] This facile introduction of an *ortho* silyl group can influence subsequent aromatic substitution reactions. Direct methanol quench of the lithium enolate derived from **6** provided the ketone **10** in which the trimethylsilyl substituent will hinder the adjacent center. The electronic character of the ring and hence the reactivity pattern can be further altered by Baeyer–Villiger oxidation of **10** to afford the acetate **11**.

Representative experimental procedure: synthesis of the enediyne acetal **9** (X=$SiMe_3$). Anhydrous



Scheme 4. Examples of tandem retro-[1,4]-Brook rearrangement/condensations. (a) Me_3SiCl, Et_3N, DMF, 75°C, 19 h, 55%; (b) *n*-BuLi, THF, −78°C, PhCHO, 30 min, 74%; (c) $CeCl_3$, THF, *n*-BuLi, **8**, −78°C, 1.75 h, 72%; (d) *n*-BuLi, THF, −78°C, 30 min; MeOH, 99%; (e) CF_3CO_2H, CH_2Cl_2, KH_2PO_4, 0–21°C, 5 days, 76%

cerium trichloride (0.41 g, 1.72 mmol) was heated at 140°C under vacuum (2 torr) for 3 h, cooled to room temperature (21°C) and then suspended in tetrahydrofuran (6 mL) to generate a white slurry (2 h, vigorous stirring). A sample of *o*-bromoacetophenone trimethylsilyl enol ether (**6**, 0.47 g, 1.72 mmol) was dissolved in tetrahydrofuran (4 mL), and cooled to −78°C. A hexane solution of *n*-butyllithium (0.69 mL, 1.76 mmol, 2.5 M solution) was added dropwise to the stirred solution. After 45 min the solution was transferred via cannula to the cerium trichloride slurry that had been previously cooled to −78°C. The solution immediately turned lemon yellow and was allowed to stir for 1 h at this temperature. The aldehyde **8** (0.25 g, 1.2 mmol, in THF, 1 mL) was next added dropwise to the organocerium solution and the reaction was monitored by TLC. After 1 h, the reaction was quenched with saturated aqueous ammonium chloride solution, partitioned between ether and brine, dried over anhydrous magnesium sulfate, concentrated, filtered and purified by column chromatography on Florisil® (1:2, ether:petroleum ether) to afford 0.34 g of the aldol product **9** (X=$SiMe_3$) in 72% yield. ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.8 (dd, ^3J=8.8 Hz, ^4J=1.6 Hz, 1H), 7.6 (m, 1H), 7.4 (m, 2H), 5.8 (bs, 2H), 5.3 (bs, 1H), 5.1 (m, 1H), 3.3–3.7 (m, 7H), 1.1 (t, ^3J=7 Hz, 6H), 0.2 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 0.1, 14.9, 46.2, 58.9, 60.8, 81.7, 82.1, 91.4, 91.6, 97.4, 118.7, 120.5, 128.6, 128.7, 129.0, 131.7, 135.8, 142.0, 200.3; IR (NaCl, neat) 3403, 3030, 2982, 1683, 1585, 1344 cm^{-1}; anal. calcd for $C_{23}H_{30}O_4Si$: C, 69.35; H, 7.53. Found: C, 69.16; H, 7.46.

In conclusion, we have established the ease and utility of the regiospecific migration of a trimethylsilyl group from the oxygen of the corresponding acetophenone enol ether to the *ortho* position of the aromatic ring. The protocol provides an alternative when standard aldol methods fail.

Acknowledgements

We are grateful to the Natural Sciences and Engineering Research Council of Canada, the Canadian Breast Cancer Research Initiative (NCI, Canada), the Saunders-Matthey Foundation for Breast Cancer Research and Torcan Chemical Ltd. for financial support of this research. S. Woo thanks NSERC for a Postdoctoral Fellowship.

References

1. (a) Brook, A. G. *J. Am. Chem. Soc.* **1958**, *80*, 1886. (b) Brook, A. G.; Legrow, G. E.; MacRae, D. M. *Can. J. Chem.* **1967**, *45*, 239. (c) Brook, A. G.; Warner, M. C.; Limburg, W. W. *Can. J. Chem.* **1967**, *45*, 1231. (d) Brook, A. G. *Acc. Chem. Res.* **1974**, *7*, 77. (e) Brook, A. G.; Bassindale, A. R. In *Rearrangements in Ground and Excited States*; De Mayo, P., Ed.; Academic Press: New York, 1980; Vol. 2, p. 149.
2. Biernbaum, M. S.; Mosher, H. S. *J. Am. Chem. Soc.* **1971**, *93*, 6221.
3. (a) West, R.; Lowe, R.; Stewart, H. F.; Wright, A. *J. Am. Chem. Soc.* **1971**, *93*, 282. (b) West, R.; Wright, A. *J. Am. Chem. Soc.* **1974**, *96*, 3214. (c) Evans, D. A.; Takacs, J. M.; Hurst, K. M. *J. Am. Chem. Soc.* **1979**, *101*, 371. (d) Eisch, J. J.; Tsai, M. R. *J. Organomet. Chem.* **1982**, *225*, 5. (e) Linderman, R. J.; Ghannam, A. J. *J. Am. Chem. Soc.* **1990**, *112*, 2392.
4. Wittig, G.; Lhmann, L. *Justus Liebigs Ann. Chem.* **1942**, *550*, 260.
5. Bailey, W. F.; Jiang, X.-L. *Organometallics* **1995**, *14*, 5704.
6. For 1,3-*C* to -*O* and 1,3-*O* to -*C* migrations see (a) He, H.-M.; Fanwick, P. E.; Wood, K.; Cushman, M. *J. Org. Chem.* **1995**, *60*, 5905. (b) Alberti, A.; Chatgilialoglu, C.; Pedulli, G. F.; Zanirato, P. *J. Am. Chem. Soc.* **1986**, *108*, 4993. (c) Shinokubo, H.; Miura, K.; Oshima, K.; Utimoto, K. *Tetrahedron Lett.* **1993**, *34*, 1951. (d) Damrauer, R.; Eaborn, C.; Happer, D. A. R.; Mansour, A. *J. Chem. Spc. Chem. Commun.* **1983**, 348. (e) Smichen, G.; Pfletschinger, J. *Angew. Chem., Int. Ed. Engl.* **1976**, *15*, 428.
7. For 1,4-*O* to -*C* and 1,4-*C* to -*O* migrations see (a) Bures, E. J.; Keay, B. A. *Tetrahedron Lett.* **1987**, *28*, 5965. (b) Bures, E. J.; Keay, B. A. *Tetrahedron Lett.* **1988**, *29*, 1247. (c) Spinazzé, P. G.; Keay, B. A. *Tetrahedron Lett.* **1989**, *30*, 1765. (d) Beese, G.; Keay, B. A. *Synlett* **1991**, 33. (e) Wang, K. K.; Liu, C.; Gu, Y. G.; Burnett, F. N. *J. Org. Chem.* **1991**, *56*, 1914. (f) Kim, K. D.; Magriotis, P. A. *Tetrahedron Lett.* **1990**, *31*, 6137. (g) Braun, M.; Mahler, H. *Angew. Chem., Int. Ed. Engl.* **1989**, *28*, 896. (h) Lautens, M.; Delanghe, P. H. M.; Goh, J. B.; Zhang, C. H. *J. Org. Chem.* **1995**, *60*, 4213. (i) Hoffmann, R. W.; Bewersdorf, M. *Tetrahedron Lett.* **1990**, *31*, 67. (j) Hoffmann, R. W.; Brüchner, R. *Chem. Ber.* **1992**, *125*, 2731.
8. For recent syntheses see (a) Evans, D. A.; Wood, M. R.; Trotteer, B. W.; Richardson, T. I.; Barrow, J. C.; Katz, J. L. *Angew. Chem., Int. Ed. Engl.* **1998**, *37*, 2700. (b) Nicolaou, K. C.; Natarajan, S.; Li, H.; Jain, N. F.; Hughes, R.; Solomon, M. E.; Ramanjulu, J. M.; Boddy, C. N. C.; Takayanagi, M. *Angew. Chem., Int. Ed. Engl.* **1998**, *37*, 2708.